Eur Spine J (2011) 20:1821–1836
DOI 10.1007/s00586-011-1799-1

ORIGINAL ARTICLE

The use of BoneWelding® technology in spinal surgery: an experimental study in sheep

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Received: 5 January 2010 / Revised: 22 March 2011 / Accepted: 8 April 2011 / Published online: 27 April 2011

Abstract The innovative BoneWelding® technology, where ultrasound energy bonds bioresorbable implants to bone, was tested for its feasibility in spine surgery and its local thermal effects. The three tested concepts consisted of implementation of a resorbable plating system, two converging polymer pins and suture anchors to the cervical vertebral bodies. Bioresorbable polylactide implants (PLDLLA 70/30) were inserted ventrally into the third and fourth vertebral body of seven sheep, of which six were sacrificed at 2 months and one sheep immediately after temperature measurements during implant insertion. Polymer screws were used as controls. Qualitative, semi-quantitative histological, and quantitative histomorphometrical evaluation showed excellent anchorage of the implants, new mineralized bone at the implant-bone interface, no inflammatory cell reaction or thermal damage to the adjacent bone in response to the novel insertion technology. The application of two converging pins, parallel inserted polymer pins, or fusion of the implant to the polymer plates did not affect the overall excellent tissue tolerance of the technology. Temperature increase during insertion was noticed but never exceeded 47°C for less than 1 s. The BoneWelding® technology was proven to be safe and easy to apply.

Keywords BoneWelding · Spine surgery · Resorbable implants · Cervical spine

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Introduction

BoneWelding® technology (WW Technology AG, Schlieren, Switzerland) is an innovative and an ultrasound-based insertion method for bonding bioresorbable and thermoplastic polymer pins into bone [1–3]. During insertion the polymer not only molds into the bone, but also melts and fuses with thermoplastic plates at the level of the drill holes, thus increasing mechanical stability toward shear forces in comparison to conventional screw-plate configurations [4–7]. Surgery time can be considerably reduced by the BoneWelding® technology, since tapping of screw holes is no longer necessary [8–10]. The BoneWelding® technology is already and clinically used in craniomaxillofacial surgery in humans (SonicWeld Rx, KLS Martin, Tuttlingen, Germany) and has largely replaced conventional screw-based osteosynthesis systems [2, 5, 11].

Polymers used for BoneWelding® are based on polylactide that have gained popularity as surgical implants also in spine surgery. Poly-L/DL-lactide 70/30 consist of 70% L-lactide and 30% D/L-lactide and show good biocompatibility [12, 13] in many tissues [14], among them nerves and dura mater [15, 16]. Due to the amorphous character of the

polymer no tissue irritating crystalline products are formed during degradation by means of hydrolysis [17, 18]. Degradation time is between 18 and 36 months [19–21].

In spine surgery resorbable polymer implants are considered attractive alternatives to conventional metallic implants for various reasons. Degradation of implants renders a second surgery for implant removal unnecessary [22]. Implant loosening of metallic implants is a clinically serious complication requiring subsequent surgical removal of these implants [23–28]. Removal of metallic implants in the spine due to instability or dislocation may leave a serious deficit leading to instability of the spine [29, 30]. For young patients, removal of metallic implants is necessary to avoid premature closure of growth plates. The fact that resorbable implants are degraded and require no second surgery is very attractive in spinal surgery from a medical, financial and psychological standpoint [22, 31, 32].

At the same time resorbable polymers may be contraindicated in cases of high mechanical load and/or movement, since degradation may be enhanced and occurring faster as new bone formation takes place, thus loosing the load bearing function of the implant prematurely. However, the degradation time of PLDLLA 70/30 fits well with the time frame of bone healing, such that new bone formation is not impaired [12, 20, 22, 33, 34]. Furthermore, their radiolucent properties are seen as an advantage for postoperative and follow-up radiographs or CT studies compared to metal implants [23, 33, 35, 36]. So far, successful implantations of PLDLLA 70/30 spinal cages in experimental sheep [37, 38] or goat [39, 40] as well as clinical application in human spines [33, 41–43] were reported. Furthermore, plates and screw systems for anterior fusion of vertebral bodies also yielded favorable results [2, 23, 33]. Last but not the least, resorbable polymers were already used as suture anchors for laminoplasty [31].

The goal of this study was to add another dimension to the use of bioresorbable polymer implants in spine surgery. The BoneWelding® technology was used for three different concepts of implant applications in the vertebral body: A pin-plate construct for bone fragment fixation, a single pin for multipurpose and angle-free anchoring and an anchor pin for suture fixation. The choice of concepts aimed to evaluate the impact of the insertion procedure with a potentially increasing risk of bone reaction with lower inter-implant distance and larger implant dimension. From this perception, the pin-plate concept was subdivided into (1) a triangular polymer plate with one single pin (mono) in a safe distance to other implants [3], (2) two parallel (duo) pins (Ø 3.0 mm) in proximity to each other (3 mm) and, (3) two converging pins (Ø 3.5 mm). These configurations seemed to represent a worst case scenario with the distal melting zones of the implants overlapping each other. The small suture anchors (Ø 1.6 mm) were not expected to mean a risk itself, but in combination with a resorbable suture thread and a polymer with a higher melting temperature than the market approved version (70/30 PLDLLA instead of 50/50 PLDLA of the SonicWeld Rx pins of KLS Martin, Tuttlingen, Germany) demand to be evaluated in the vertebral body.

The study was based on the hypothesis that BoneWelding® technology is suitable and even advantageous for all three concepts of spinal implants for ease of application. In addition, it was also hypothesized that neither the combination of duo pins in close vicinity nor fusion of plate and pins during insertion would cause thermal damage to the bone and thus, jeopardize the overall safety of the innovative technology.

Materials and methods

A bioresorbable Co-Polymer L-lactide and DL-lactide was used in this study. The polylactide acid (PLA) consisted of 70% L-lactide and 30% DL-lactide (Resomer® LR708, Böhringer Ingelheim, Germany). Several types of implants were used as depicted in Fig. 1.

Screw/pin-plate fixation (group A):

Triangular plate. The dimensions of the triangular plate were 19.5 mm in length, 12.5 mm in width and 2.0 mm in thickness. The distance between the centers of both holes

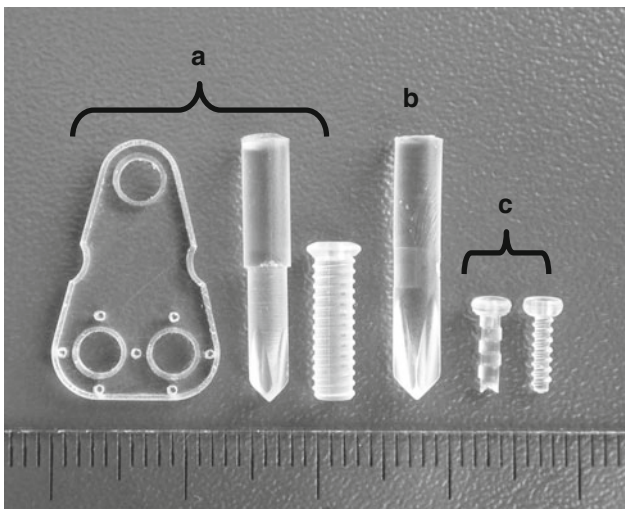

Fig. 1 The picture shows the implant system **a** Pin-plate system (group A) of a triangular plate, BoneWelding® pins and screws as control; **b** BoneWelding® pins (3.5 mm diameter) for double impact converging insertion (group B); **c** BoneWelding® pin and a screw type control type suture anchors (group C)

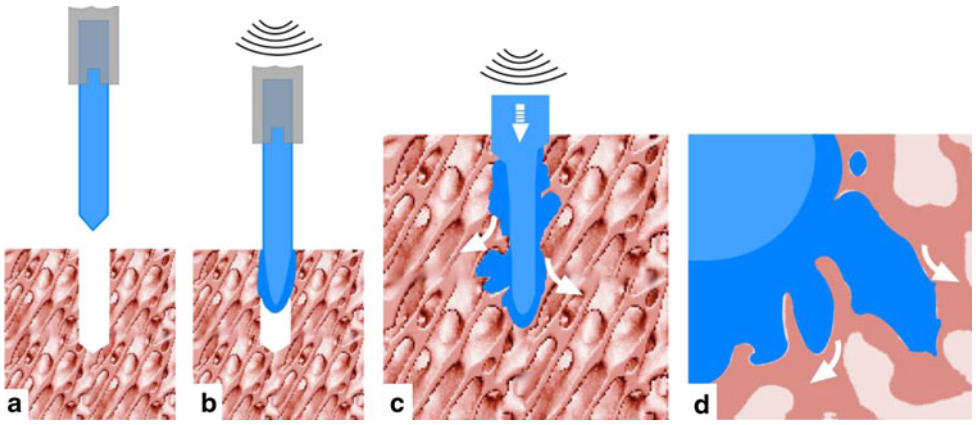

Fig. 2 The figure explains the BoneWelding® technology principle **a** polymer pin attached to the ultrasound device ready to be inserted in prepared drill hole; **b** friction due to ultrasound causes phase-changes (solubilization) at the surface of the implant and contact to bone; **c** melted polymer intrudes into bone cavities; **d** seconds after ultrasound application the polymer hardens and creates large contact area to bone, which is the reason for the immediate and excellent biomechanical implant stability

in the base was 5.5 mm. Four equally distributed holes of 0.5 mm diameter were placed around these larger screw/pin holes at a 90° angle serving as guide holes for thermocouples. The two 3/8 circular impressions on the plate were designed for attachment of grip holders. The plate was fixed with either PLA screws or pins through the 3.2-mm holes to the ventral side of the cervical vertebrae.

The 3.0-mm polymer pins were cylinders with grooves at the conical tip. The pin had a wider end part that formed the connection to the ultrasonic instrument. The connection was cut-off after ultrasonic insertion. The diameter and amount of material of the polymer pin were constructed such, that after bone welding the centripetal dimension was similar to the polymer screw.

The *3.2-mm screw* (3.2 mm diameter, 12.0 mm length) served like the polymer pin for fixation of the triangular plate to the bone.

Convergent implantation (group B)

The *3.5-mm pin* had a diameter of 3.5 mm throughout, but otherwise was similar to the 3.0-mm pin.

Suture anchors (group C)

The *suture anchor polymer pin* was also cylindrical in form with a shaft length of 6 mm and a diameter of 1.6 mm. Shaft was designed in 6 trilobules. The tip (Ø 1.4 mm) was dove-tailed to take-up the suture thread before ultrasonic insertion.

Suture anchor screws were more or less identical to the suture anchor pin (7 mm length, 1.6 mm diameter with a conical tip diminishing the diameter to 1.0 mm). The head was 3.2 mm in diameter with a height of 1 mm.

Ultrasound device

Depending on the size of the implants different ultrasound devices had to be chosen. For the larger polymer pins (Group A and B) an ultrasound device was used that works with a frequency of 20 kHz and maximal power of 150 watts (Branson "LPe", Branson Ultrasonics SA, Carouge, Switzerland). Instead, the 1.6 mm PLA-pins (Group C) were inserted using a Sonic Welder Rx (KLS Martin, Tuttlingen, Germany, 29.5 kHz, max. power 20 watts). At insertion the ultrasound devices transmit their energy to the polymer implants such that they start to vibrate (Fig. 2). The energy delivery has to be adapted to the size of the implants and the insertion conditions, since otherwise melting of only the surface cannot be maintained.

Study design

A total of seven adult, female Brown Headed Mutton sheep were used ranging from 63 to 103 kg (mean 87.5 kg) body weight and 1.5–3.5 years of age (mean 2.8 years). Six sheep were observed for 8 weeks after implantation, while one sheep was immediately euthanized still in anesthesia after temperature measurements during insertion of the implants. Implants were inserted in the third and fourth cervical vertebrae of each sheep. Of the six surviving sheep three animals were used to introduce the triangular plates (group A) while the other three sheep received implants of groups B and C. The one sheep used for the acute terminal experiment of temperature measurement received all implants of group B.

All animal experiments were performed according to the principles of laboratory animal care (NIH publication No. 86-23, revised 1085) and Swiss laws of animal welfare and

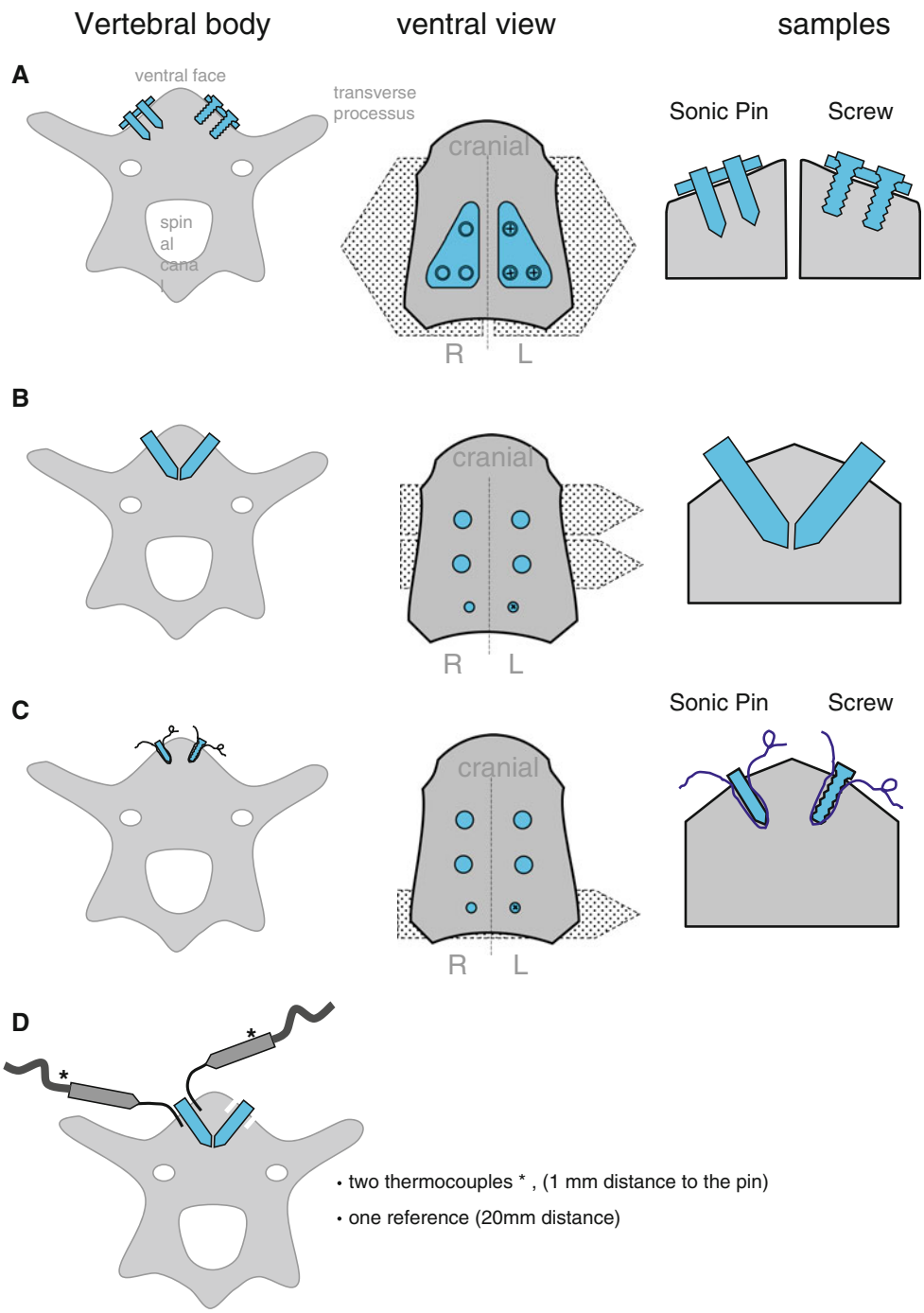

Fig. 3 The schematic drawing pictures the implant concept **a** triangular plates, mono- and duo screws of group A; **b** converging pins of group B; **c** suture anchors of group C; arrangement of thermocouples around pins of group D

were authorized through the local federal authorities (authorization # 137/2006). The distribution of implants between vertebrae and animals was made according to the three concepts of implant insertion (Fig. 3; Table 1).

Management of sheep

All sheep were chosen from our laboratory's own sheep herd, which is routinely checked for its health status. Ten days before surgery sheep were adapted to their new environment close to the surgical facilities. Prior to surgery sheep were fasted for 24 h with water ad libitum.

Surgery

Sheep were routinely sedated and anesthetized [xylazin (Rompun®; 0.1 mg/kg KGW i.m.; Bayer, distributor Provet AG, Uznach, Switzerland; ketamine (2 mg/kg KGW, i.v., Narketan®, Vetoquinol AG, Belp- Bern, Switzerland); diazepam (0,1 mg/kg KGW, i.v.; Valium®; Roche Pharma

Table 1 Distribution of implants and groups including subgroups are listed

Group	Subgroups	Implant	Distribution	No. of implants	Sheep
A	A1	PLA-pin Ø 3.0 mm	2 pins parallel through triangular plate	12	2236
Plate fixation: triangular plate fixed with	Duo pin				2237
					2238
PLA-pins					
PLA-screws					
	A2	PLA-screw Ø 3.0 mm	2 screws parallel through triangular plate	12	2236
	Duo screw				2237
					2238
	A3	PLA-pin Ø 3.0 mm	1 pin singular through triangular plate	6	2236
	Mono Stift				2237
					2238
	A4	PLA-screw Ø 3.0 mm	1 screw singular through triangular plate	6	2236
	Mono screw				2237
					2238
B		PLA-pin Ø 3.5 mm	2 converging pins	24	2239
Converging pins					2240
					2241
C	C1	PLA-pin Ø 1.6 mm	1 pin single with suture	6	2239
Suture anchors	Suture anchor pin				2240
					2241
	C2	PLA-screw Ø 1.6 mm	1 screw single with suture	6	2239
	Suture anchor screw				2240
					2241
D		PLA-pin Ø 3.5 mm	2 converging pins	8	2242
Temperature measurements					

AG, Reinach, Switzerland); propofol (Propofol®-Lipuro, 2–4 mg/kg KGW, i.v., 1% glass ampules B. Braun, Melsungen AG, Germany) and maintained with inhalation (isoflurane to effect (Florene®, Abbot AGA, Baar, Switzerland)]. Analgesia was maintained for 4 days [Carprofen (4 mg/kg KGW i.v.; Rimadyl®, Pfizer, Dr. Gräub AG, Bern, Switzerland; Buprenorphin (0.01 mg/kg; i.m.; Temgesic®; Essex Chemie AG, Lucerne, Switzerland)], while perioperative prophylactic antibiotic and analgetic therapy consisted of benzylpenicillin (30,000 IU/kg KGW i.v., Penicillin "Grünenthal 10 Mega"; Grünenthal GmbH, Aachen, Germany), Gentamycin (6 mg/kg KGW; i.v., Vetagent®, Intervet, Veterinaria AG, Zürich, Switzerland).

The sheep were placed in dorsal recumbency with the head and neck slightly overstretched dorsally to expose the ventral aspect of the cervical vertebrae. A routine approach with paramedian and blunt dissection between the sternohyoid and sternomastoid muscles allowed direct access to the ventral aspect of the cervical vertebral bodies.

The *PLA-triangular plate-pin combination* (Group A) was placed on the left side of the ventral crest of the vertebral body using custom made drills and plate guides. A sleeve was inserted to drill a 2.5-mm drill hole with 10.0-mm depth. A metal pin was inserted securing the plate to the bone while the second, respectively, third holes, were drilled. The plate and drill guide was removed and the cortex opened using a 3.2-mm drill, thus, creating a stepped drill hole. This was done to move the major melting zone of the polymer pins from the cortical to the cancellous bone. A special plate holder facilitated keeping the triangular plate in place. The metal pins were again used to secure the position while the three pins were inserted. The depth of pin insertion was controlled through adding a mark at 10.0 and 12.0 mm measured from the tip of the pin. A pin cutter was used to shorten the inserted pins to a level where they protruded ca. 2 mm above the plate. The same procedure was repeated on the left side of the fourth cervical vertebra.

The triangular plate–screw combinations (group A) were placed on the right side of the third and fourth cervical vertebrae in a similar pattern except that a 2.7-mm drill bit was used to drill the 10.0-mm deep holes and a 3.2-mm tap to cut the threads before the screws could be inserted with a screw driver.

Two pairs of *converging implants* of (Group B) were implanted per vertebra, in C3 and C4, in the cranial and middle aspect of the cervical vertebra with the most proximal pins at 5.0 mm distance caudally to the proximal border of the bone to avoid penetration into the disk space. A custom-made drill guide allowed symmetrical positioning of the two converging pins at a 70° angle from both sides of the vertebral body with the medial crest as division. Drill holes of 6.0 mm depth were prepared with a 2.7-mm drill bit. Again metal pins were inserted to guarantee placement of the drill guide while drilling the second hole. The drill guide was removed and the cortex opened using a 3.5-mm drill, creating a stepped drill hole. The insertion procedure was analogous to the pins of group A, and the protruding pins were cut also at a 2-mm distance from the bone surface.

After creating a stepped drill hole (1.4 mm to open the cortex, 1.0 mm for the distal shaft, drill depth 8 mm), the *suture anchor pins* were mounted on the ultrasound device (Sonic Welder Rx; KLS Martin, Tuttlingen, Germany). Thereafter, the suture thread (Polyglactin, Vicryl®, CT-2 plus, V333; Johnson & Johnson Intl., Brussels, Belgium) was placed in the groove at the tip of the pins and introduced into the drill hole with the pin. Drill holes of 8-mm depth were prepared with a 1-mm drill bit. During the insertion process the suture was molded into the pin. The rest of the suture was cut and excessive polymer material at the side of the pinhead removed with a scalpel blade. Instead, *the suture anchor screws* were inserted after tapping of the drill hole and tightened. Also here, the remaining suture material was cut.

The wound was closed through suturing the plane between the sternohyoid and sternomastoid muscles and subcutaneous tissue in a continuous pattern using resorbable suture material (Polyglactin; Vicryl® 2/0; Johnson & Johnson Intl., Brussles, Belgium). The skin was closed with staples (Davis + Geck Appose ULC®; B. Braun Aesculap AG, Tuttlingen, Germany).

Postoperative management

Postoperative ventrodorsal radiographs (mobile X-ray machine; KV: 74; 2.5 mAs) of the cervical spine were taken with the animals still in anesthesia to identify the positions of the various implants. The animals were kept in groups of three in small stalls for 10–14 days, when also skin staples were removed. Thereafter, they were allowed to roam in the pastures for 2 months until sacrifice. They were slaughtered at the University's own slaughterhouse.

Harvesting and preparation of bone samples

After slaughter the cervical spine was harvested and inspected macroscopically for signs of inflammation or other changes. Surgery sites were documented photographically (Digital-Foto Sony® DSC–R1, Sony Corporation) as well as qualitatively evaluated. Thereafter, ventrodorsal and lateral radiographs of the spinal column were taken (55 kV, 5 s, 3 mA; Faxitron X-ray systems, Hewlett Packard, Mc Minnville Division, Oregon, USA). Using a special band saw (Kolbe Maschinentechnik GmbH, Elchingen, Germany) the implants and adjacent bone tissue were excised and a custom-made holding device fixed in a minitome (Minitom, Precision saw, Struers A/S, Ballerup, Denmark) was used for cutting the bone specimens in a parallel plane to the implants. Additional faxitron radiographs in two planes were taken (35 kV, 9 s, 3 mA) to detect possible sclerosis and/or bone resorption adjacent to the implants. Bone blocks were fixed in 4% buffered formaldehyde for 1 week before further preparation for histology as non-decalcified specimens and embedding in methylmetacrylate [methacrylacid-methylester (Fluka Chemie GmbH, Buchs, Switzerland), dibutulylphtalat (Merck-Schuchard® OHG, Hohenbrunn, Germany), Perkadox 16 (Dr. Grogg Chemie G, Stetten, Switzerland)] [44, 45]. Blocks were finally mounted (Technovit, Leica Instruments GmbH, Nussloch Germany) on plastic frames that allowed sectioning in a precision saw (Leica® SP1600, Leica Instruments GmbH, Nussloch, Germany).

Ground sections (30–40 μm) and thin sections (5 μm) of group A were cut in three different planes (Fig. 4). The implants of group B were cut once in the longitudinal axis of both pins of the pair. Implants of group C were cut in the transverse axis. Before the 400-μm sections were glued (Cementit® CA 12; Merz + Benteli AG, Niederwangen, Switzerland) to the Acropal slides, microradiographs were taken using a high-resolution film (Fuji Photo Film Co.®, Ltd. Tokyo, Japan) and the faxitron equipment (27 kV, 11 s, 3 mA).

Ground sections were etched with formic acid and surface stained with toluidine blue, whereas thin sections were deplastified with methoxyethylacetate (Merck AG, Switzerland) and then stained either with toluidine blue, hematoxylin/eosin, or von Kossa/McNeal tetrachrome.

Ground and thin sections of group B were cut also longitudinally using the precision saw. The ground sections allowed the histological evaluation of the two converging pins at the tip. *Specimens of group C* were placed with their cranial part "face-down" into the Teflon molds and cut in a transverse plane at 2 mm distance. Ground and thin sections were cut in the same plane.

Histological evaluation

Qualitative, semi-quantitative and quantitative (histomorphometry) evaluation of histological sections was

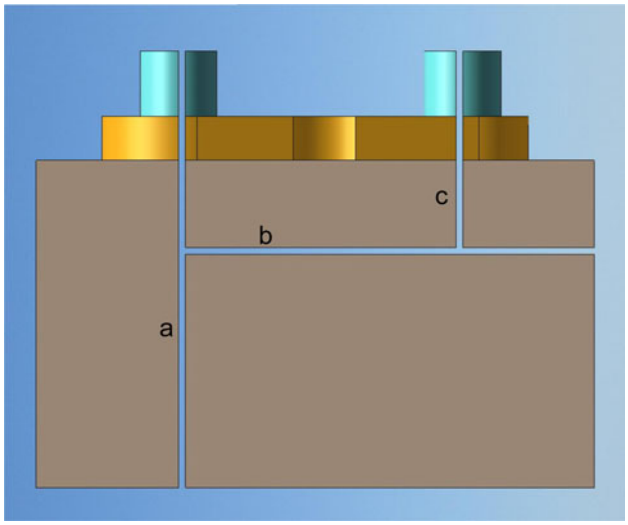

Fig. 4 The diagram illustrates the planes of sectioning for histology of group A: **a** longitudinal section through duo pins/screws; **b** transverse section of mono- and duo pins/screws; **c** longitudinal section through mono pins/screws

performed using a light microscope (MDL 404097, Leica® Instruments GmbH, Nussloch, Germany).

Evaluation variables using the thin sections included new bone formation, implant positioning and degradation, tissue reaction of adjacent bone and fibrous capsule formation. In addition, positioning of the implant within the transverse foramina and structures thereof, such as the vertebral vessels and nerves (a., v., n. vertebralis) was studied. Surgery related damages to the latter structures were assessed in thin sections stained with HE. The degree of mineralization was assessed in thin sections stained with van Kossa/McNeal. Scores for semi-quantitative evaluation were given for insertion (0 = incomplete, 1 = complete), positioning of the implant in vertebral foramen (0 = no, 1 = yes) and grade of mineralization (0 = <70%; 1 = 70%; 2 = 80%; 3 = 90%; 4 = 100%).

Cellular reaction to the implants was assessed semi-quantitatively using the thin sections stained with HE. Thin sections were viewed in a 40× magnification and scores were given for presence, respectively, absence of cells. Focus was placed on polymorph nuclear granulocytes, lymphocytes, plasma cells, macrophages and giant foreign body cells. If available, four compartments were evaluated: the bone-implant interface (I); the remodeling zone (II), bone-fibrous tissue contact zone (III) and fibrous tissue adjacent to the implants (IV). Numbers of cells within the different compartments were scored according to ISO 10993-6 (2007) with 0 = none, 1 = 1–5 cells, 2 = 6–10 cells, 3 = 11–15 cells, 4 = 16–50 cells and 5 = >50 cells/implant.

Histomorphometrical evaluation was performed on ground sections using a macroscope (Leica® M420, Leica-microsystems, Glattbrugg, Switzerland), where a digital camera was mounted (Leica DFC 320®). Each implant was photographed and computed using the appropriate software (Leica IM 1000®) in TIF format (2,088 × 1,400 Pixel). An overview of the implants and the adjacent bone was captured in addition to the bone section between the implants and the tips of the converging pins/screws of group B. The extent of bone remodeling in longitudinal and transverse sections was also measured using measurement tools integrated in the image database software (Fig. 5). The bone remodeling distance was defined as the distance between drill hole edges and the most distant remodeling or new bone formation around the implant. In case of double implants [duo-implants (Group A) and converging pins (Group B)] the central area between the two implants was measured separately. Additional measurement of the width between the implants was performed, where the two central remodeling distance lines were crossing. The distance between the duo pins/screws of group A was quantified by measuring the entire distance between the drill hole edges.

Statistical evaluation

Statistical analyses were performed using the software program SPSS® (MacIntosh, OS X, Version 16.2, Chicago, IL). The quantitative histomorphometrical data and the semi-quantitative scores were subjected to parametrical factorial analysis of variance (ANOVA), where overall differences between groups were assessed. The post hoc tests according to Scheffé and Bonferroni allowed evaluating individual differences between groups. p values <0.05 indicated statistically significant differences.

Temperature measurements

The temperature increase within the adjacent bone was measured in vivo (8 trials) during insertion of the 3.5 polymer pins (group B) using one sheep in a terminal experiment. The surgical procedure was identical to all other sheep, except that two extra-drill holes with a diameter of 0.55 mm for insertion of the thermocouples were made at 1.0 mm distance to the pins. A special, custom-made drill guide was prepared, which could be inserted in the previously prepared drill hole for the pins. The 0.55 mm drill holes for the thermocouples were placed at 180° to each other. The small thermocouples (covered thermocouples type J, Ø 0.5 mm, IEC 584, Class 1, Roth & Co, Oberuzwil, Switzerland) were inserted before welding of the pins. A reference 0.55 mm drill hole was created in a vertebra at 15 cm distance to the site of pin insertion. The thermocouples were connected to a datalogger (Data Acquisition Unit Agilent 34970A, Agilent Data Logger Software v.3 on MS Windows XP, Agilent Technologies,

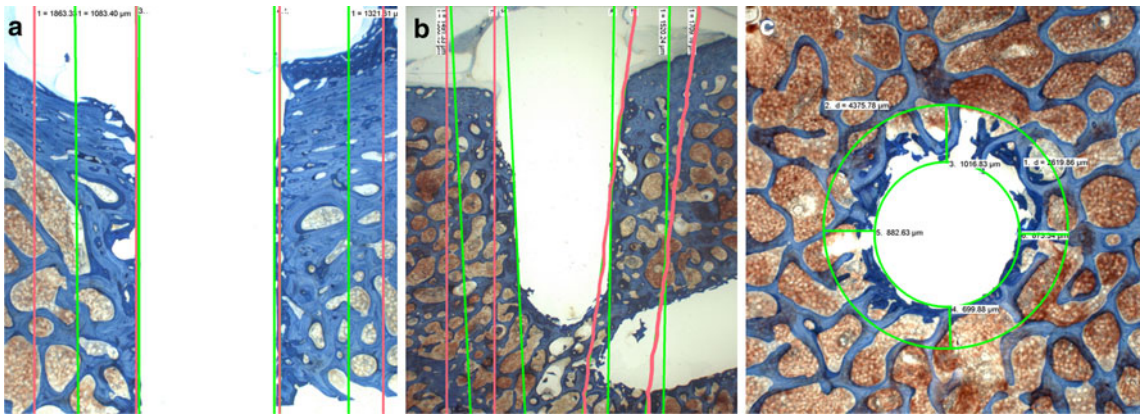

Fig. 5 The histology sections show the measurement lines for histomorphometrical evaluation of the maximal bone remodeling distance: *Lines* **a** for conical pins/screws (group A), **b** converging pins (group B), and **c** for transverse section of implants of all groups. *Pink lines* mark the boundary of cortical remodeling, *green lines* the boundary of trabecular bone remodeling

Inc., Santa Clara CA, USA) that was equipped with a specific software program (Agilent Data Logger Software v.3 on MS Windows XP). Ten measurements per second were acquired and the following parameters were studied: duration of ultrasound application (t ultrasound), duration until maximal temperature increase was reached (t to DT max), maximal temperature difference (DTmax) and temperature difference after 60 s. (DT60sec). Median values including standard deviations were calculated and graphically displayed as boxplots.

After all pins were inserted the animals were sacrificed under anesthesia and the spine was harvested. Each sample was divided in half through the center of the pins to evaluate polymer distribution to the adjacent bone. An attempt was made to divide the samples in the plane of the small drill holes of the thermosensors. Thereafter, the surface of the bone was surface stained with toluidine blue.

The temperature measurements were also performed ex vivo in a similar setup in fresh cadaver material as described elsewhere [46, 47].

Results

Surgery

All animals could be operated without complications. The custom-made instruments (WW Technology AG, Switzerland) guaranteed precise and repeatable positioning of all implants. Generally, the BoneWelding® technology allowed faster insertion compared to the screw controls, since no additional tapping was required. In three instances (1 group A, 2 in group B) a second pin had to be ultrasonically inserted since melting did not occur at the first instance. When pins were replaced insertion went smooth and without complications.

Insertion of pins of *group A* and *B* went smooth and pins welded nicely not only into the bone but also with the plate. Insertion of screws was routine. Implantation of suture anchors (group C) caused more problems. This was true for both, the pins and screws. While the small pins were diverted in their direction in cases of complication, breakage of the screw heads occurred during insertion (5/6). The suture material caused a narrowing of the drill holes that resulted in increased force application with the screwdriver and subsequent breakage of the screw head. Nevertheless, two suture anchors either with a pin or screw could be inserted in each vertebral body without complications. The 3.5-mm pins of *group D* (measurements of temperature) could also be inserted without problems. However, after successful insertion, in two instances the pins could not be detached easily from the ultrasound instrument and had to be cut.

Postoperative phase

All animals recovered without complications and ambulated without signs of neurological deficits. Small seromas were present at the ventral aspect of the wound during the first days after surgery. However, they subsided within a week and primary wound healing was achieved in all animals.

Radiographs

Postoperative radiographs showed correct positioning of pins and screws in all animals. Since the polymer implants were invisible in radiographs, positioning was determined according to the position of the drill holes. No changes of bone density or structure could be detected in the vertebral bodies. In contrast, a radiodense line of 0.5 mm width indicating new bone formation was observed around the

implants at the time of sacrifice in groups A and B, although in group B this line was more visible at the peripheral aspects of the converging pins. Drill holes of group C were barely identifiable. In one sheep a slight callus was recorded at the ventral aspect of the most caudal and cranial vertebral body.

Macroscopic evaluation

Macroscopic appearance was uneventful in all instances such that no signs of inflammation were present at the time of sacrifice (Fig. 6). The pins and screws of *group A and B* were all firmly seated in the vertebral bodies. The implants could easily be located and cleansed from the tissue before further processing for histology. Instead, the suture anchors were much harder to find. 4/6 pins and 2/6 screws were located as an entity and cut as anticipated. Nevertheless, the transverse sections of the suture anchors could be cut in the correct plane. The vertebrae of *group D* could be cut longitudinally and polymer infiltration into the adjacent cancellous structure was easily visible, especially at the transition between cortex and cancellous bone. The polymer filled mostly the adjacent bone marrow cavities close to the implant.

Microradiographic evaluation

Microradiographs revealed identical patterns in radiodensity as found in new bone formation of ground sections stained with toluidine blue. Also, calcification of new bone could be confirmed right up to the implants. Therefore, separate evaluation of microradiographs was not performed.

Histology

Qualitative evaluation

Bone formation and remodeling at the implant surface was observed along all implants. Due to solubilization of the polymer during preparation (infiltration with methylmetacrylate) the implants themselves were not always present or visible within the bone samples. However, since preservation of the adjacent tissue in its original structure is maintained in plastic sections, their margins could easily be identified in ground and thin sections. Direct contact between implant and bone was normal. While samples with screws showed a clear interface between the original thread and bone, respectively, fibrous tissue, infiltration of the polymer into the adjacent structures was seen in samples with bone-welded pins and most prominent with the 3.5-mm pins of group B (Fig. 7). Opened bone marrow cavities that were not filled with polymer were usually filled with new woven bone (Fig. 8a–c). Insertion of pins/screws of group A was not always complete (ca. 2–3 mm protrusion)

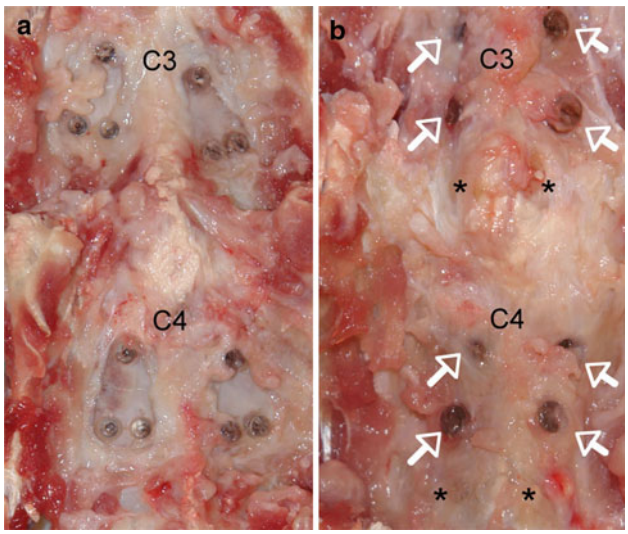

Fig. 6 Macroscopic appearance of implants at the ventral aspect of the third (C3) and fourth (C4) cervical vertebral bodies after sacrifice shows no signs of inflammation. **a** Triangular plates with welded pins at the left and screws at the right were firmly seated in the vertebral bodies. **b** Also polymer pins of group B were stable and easily identifiable (*arrows*). Suture anchors pins and screws of group C were already partially overgrown by periosteal bone formation (*asterisk*)

for duo pins (5/12) and screws (1/12), whereas the mono pins/screws were always completely inserted. There, significant differences were found between 3.5 and 3.0 mm PLA-pins ($p = 0.015$). Insertion completeness could not be assessed in the transverse sections of the suture anchors. Two laterally placed duo pins extruded ventrally at the transverse processes into the fibrous tissue. In addition, half of the pins and screws of group A were protruding into the transverse foramina of the vertebral bodies with their tips. These foramina showed a denser granulation tissue and less fat cells compared to their counterparts, where no implant tip was positioned. However, in all cases the vertebral veins, arteries and nerves were still intact. Granulation tissue was found close to the tips each, a screw and a pin, and in two cases the medial layer of the artery or nerve tissue showed vacuoles (1 pin/1 screw).

With all implants no fibrous capsule or signs of bone necrosis were found. Degradation of the implants was also not demonstrated. In thin sections stained with von Kossa/McNeal mineralized bone was observed at the bone-implant interface with the implants of all groups.

Histomorphometrical evaluation

Mean values with standard evaluations are depicted in Table 2. The width of the bone remodeling area was highest in implants of group B, where the central cortex in between the two pins was significantly more remodeled compared to the other duo-implants ($p < 0.0001$). Furthermore, the 3.5-mm pins of group B showed a significant higher remodeling

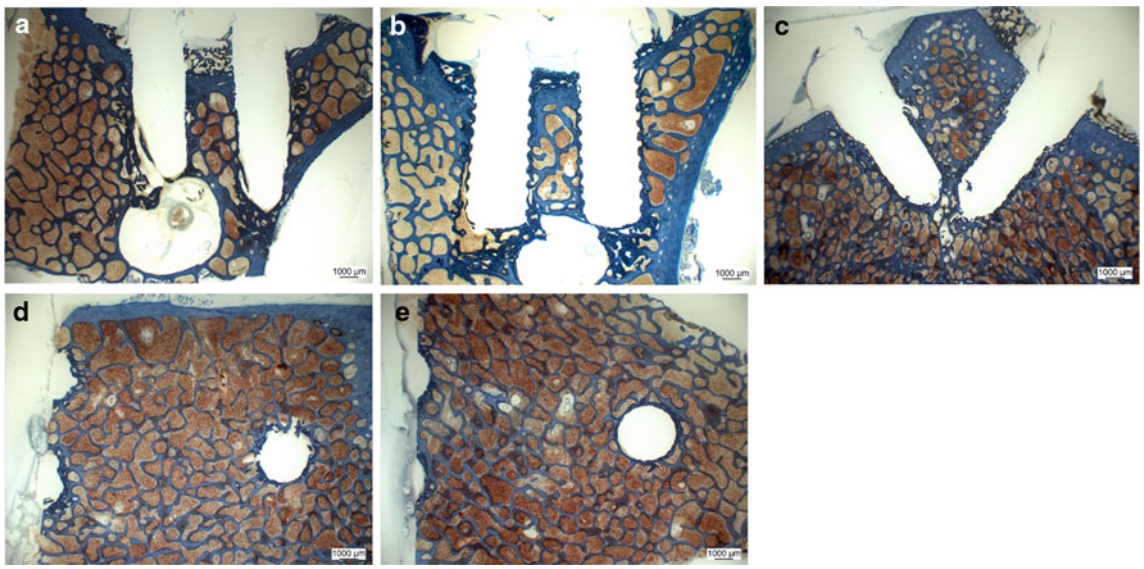

Fig. 7 Longitudinal sections through duo pins (**a**) and screws (**b**) of group A show good implant integration in vertebral bodies and are easily distinguished by clear threads in case of screws. The converging pins (group B) reveal excellent positioning and good infiltration with polymer (c) Transverse sections of duo and mono pins (**d**) and screws (**e**) show similar good new bone formation immediately adjacent to the implant surface

area at the peripheral cortex compared to the duo pins ($p = 0.042$) and duo screws ($p = 0.025$). The mean values of the duo pins and screws of group A were very similar. Also with the single pins/screws of group A no differences were found, although the pins showed a tendency for increased cortical remodeling. The central cancellous bone between the converging pins of group B showed a similar pattern such that the remodeled area width was significantly higher compared to the duo pins and screws of group A ($p < 0.001$). Again, the values between the duo screws and pins of group A did not differ. The width of remodeled bone around the 3.5-mm pins of group B was also significantly higher in comparison to all other groups ($p < 0.0001$), except to the group of the suture anchor pins, where differences were less significant ($p = 0.021$). The only groups that were not significantly different to the converging pins of group B were the suture anchor screws. No statistically significant differences were found in all other groups, although there was a tendency for the single pins and screws of group A to be lowest, whereas all other groups were settled between the converging implants of group B and the single pins of group A.

The width of the central space between the converging pins of group B at the meeting points of the remodeling lines was 4.0 ± 0.9 mm, and 2.9 ± 0.5 mm for the duo screws and 3.1 ± 0.4 between duo pins of group A.

Histology, semiquantitative evaluation of cellular reaction

The mean values of the four evaluated compartments were low (mean score < 1) and similar in all cases. Therefore, in this report only mean values of all four compartments are presented in most instances (Table 3). No basophilic *granulocytes* and also very few neutrophils were present such that most scores reflect the presence of eosinophilic granulocytes. Often the granulocytes were found within or close to vessels. The highest values were found for the suture anchors of group C (pins/screws), followed by the converging pins of group B and duo pins of group A. The lowest values were found for the mono screws of group A. *Lymphocytes* were variable within the four compartments showing the highest scores in compartment A (bone-implant contact) for mono pins/screws and the converging pins. Statistically significant differences were found between mono pins and duo pins of group A ($p = 0.017$). Nevertheless, the mean values of lymphocytes in all four compartments were very low for all implants, again, with the highest scores for the suture anchors (pin and screws) of group C. The scores for *plasma cells* were very low in all groups with zero values for the suture anchor groups of group C. Mean values for *macrophages* were also low and generally <1. Only in compartment D higher values were recorded for converging pins of group B. In compartment B statistically significant differences were found for mono pins and screws of group A compared to the other groups ($p < 0.031$). The highest scores were found for mono pins and screws of group A followed by the converging pins of group B, duo pins and screws and last the suture anchors (pins/screws). Hemosiderin was identified in macrophages of the converging pins as a result of erythrocyte degradation. Also scores for *giant foreign body cells* were low (<1). The highest values were found for the suture anchors.

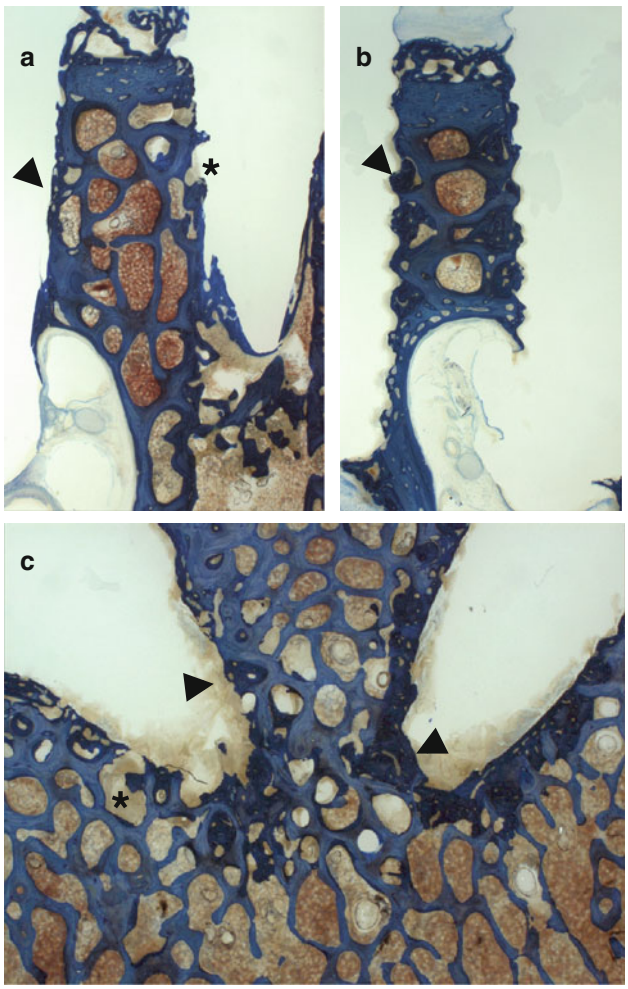

Fig. 8 Close-up view of adjacent new bone with the implants of group A and B shows excellent new bone formation (dark bone matrix) within the bone marrow cavities, where no polymer intruded (*arrowheads*). When polymer was present (*asterisk*) new bone formation was less pronounced and limited to the trabecular surface. Pictures represent **a** the duo pins, **b** the duo screws of group A and **c** converging pins of group B

Temperature measurements

Measuring of temperature during pin insertion went without complications. The maximal temperature increase during insertion was 11.3 ± 3.7°. The bone temperature was 4.0 ± 2.5°C higher at 60 s after beginning insertion. The duration of insertion was 2.5 ± 0.3 s and the bone reached its maximal temperature after 4.8 ± 1.5 s (Fig. 9).

Discussion

This study demonstrated that bone BoneWelding® technology can successfully be used also in spine surgery and thus for variable concepts. Ultrasound insertion of 3.0 mm mono or duo pins in combination with a triangular plate, or as 3.5 mm converging pins were well tolerated by the adjacent vertebral bone, even when pins were positioned close to each other. Furthermore, insertion of small suture anchors in combination with a suture thread showed that the suture material could be well kept in place by melting into the polymer. Last but not the least, temperature measurements during ultrasound insertion of 3.5-mm pins recorded a maximal temperature increase of 11.3°C, and for only a very short time (<1 s). Temperature increase never exceeded 47°C.

Three different concepts for the use of BoneWelding® technology in combination with biodegradable implants in spine surgeries were investigated in this study. While biodegradable implants per se are already used in other experimental studies [22, 38, 48, 49], as well as clinically in humans [23, 33, 34, 50, 51], fixation of these implants is still based on more conventional techniques as preparing drill holes with a tap for insertion of—in this case also mostly—degradable screws. The use of BoneWelding® technology was already reported successfully in the tibia using polymer pins and metal pins enhanced with polymer anchorage [3, 46, 47], or also dental implants [1]. However, this is the first report of using this technology for spinal implants. The three different concepts that were followed with applying BoneWelding® technology in spine surgery were based on already used clinically successful systems of resorbable polymer implants [31, 34, 38, 52]. Therefore, the focus of this study was placed not on the implant materials or biomechanics of using such implants, but on different impact levels and related risk considerations of the innovative and clinically very attractive insertion technology. Ultrasonic fusion of implants (group A), bone (pins) and suture material for spinal surgery was novel and, as results demonstrated, safe to use and did not interfere with bone healing or implant fixation.

Sheep served well as experimental animals in this study in many aspects. Most important issues are the size of the animals and their similar bone metabolism. The use of two adjoining vertebral bodies was easily possible and did not interfere with results, but allowed reduction of animal numbers while still receiving statistically meaningful data. The time point of 2 months was selected based on earlier experiments, where new bone formation and biocompatibility and osseointegration issues or consequences of bone necrosis could be easily studied [3, 53, 54].

As for the surgical procedures, the BoneWelding® technology proved successful also for indications in the spine. In fact, application of the pins inserted with ultrasound was faster and technically easier compared to screws, where drill holes needed tapping before insertion of the screws. The technical procedure for the implantation of the triangular plate was well conceived and allowed

Table 2 Mean values of the histomorphometrical evaluation are given

Subgroup	Group	Width of remodeled bone (mm)			
		Cortex central	Cortex periphery	Cancellous bone central	Cancellous bone periphery
A1 Duo PLA-pin	A	1.18 ± 0.4	1.35 ± 0.2	1.11 ± 0.3	1.22 ± 0.3
A2 Duo screw	A	1.22 ± 0.1	1.33 ± 0.2	1.13 ± 0.2	1.24 ± 0.3
A3 Mono PLA-pin	A		1.77 ± 0.2		1.12 ± 0.2
A4 Mono screw	A		1.55 ± 0.1		1.12 ± 0.2
B PLA-pin (Ø 3.5 mm)	B	1.79 ± 0.4	1.79 ± 0.6	1.75 ± 0.5	1.72 ± 0.4
C1 Suture anchor pin	C				1.22 ± 0.2
C2 Suture anchor screw	C				1.44 ± 0.4

Note that the width of remodeling could not be measured with all implants, since due to the section plane not all structures were visible (e.g. cortex)

Table 3 Mean values of the semiquantitative evaluation of cellular reactions to the implants are presented

Subgroup	Group	Mean values of cellular reaction scores				
		Polymorph nuclear granulocytes	Lymphocytes	Plasma cells	Macrophages	Giant foreign body cells
A1 Duo PLA-pin	A	0.38 ± 0.9	1.08 ± 1.2	0.15 ± 0.4	0.67 ± 1.0	0.29 ± 0.4
A2 Duo screw	A	0.15 ± 0.7	0.44 ± 0.8	0.08 ± 0.3	0.77 ± 0.8	0.50 ± 0.7
A3 Mono PLA-pin	A	0.21 ± 0.5	1.13 ± 1.0	0.04 ± 0.1	0.96 ± 0.4	0.25 ± 0.4
A4 Mono screws	A	0.00 ± 0.0	1.33 ± 1.1	0.04 ± 0.1	1.25 ± 1.0	0.17 ± 0.3
B PLA-pin (Ø 3.5 mm)	B	0.46 ± 0.1	1,19 ± 1,0	0.03 ± 0.1	0.89 ± 1.0	0.67 ± 0.7
C1 Suture anch. PLA-pin	C	0.67 ± 1.2	1.33 ± 1.6	0.00 ± 0.0	0.08 ± 0.2	0.67 ± 0.1
C2 Suture anch. screw	C	0.84 ± 1.6	1.59 ± 1.8	0.00 ± 0.0	0.34 ± 0.3	0.75 ± 0.5

Note that all scores are very low and thus, overall biocompatibility of implants is very high

accurate positioning of the pins or screws. The same was true for the other implants of group B and C. Furthermore, insertion of suture anchors caused breakage of the head due to excessive torque when screws were inserted with the suture material in place. Instead, suture threads incorporated smoothly into the melted polymer. Breakage of screw heads had already been reported as a problem using polymer screws, even without the additional challenge of introducing suture material at the time of screw insertion [2]. The incomplete insertion of some of the mono- or duo pins of group A could be due to several reasons, of which the most simple could be that the surgeon stopped ultrasound application too early. It could also be that melting and fusion of the pins to holes of the triangular plate inhibited further insertion of the polymer implant. Since this never occurred with correct application in vitro, we

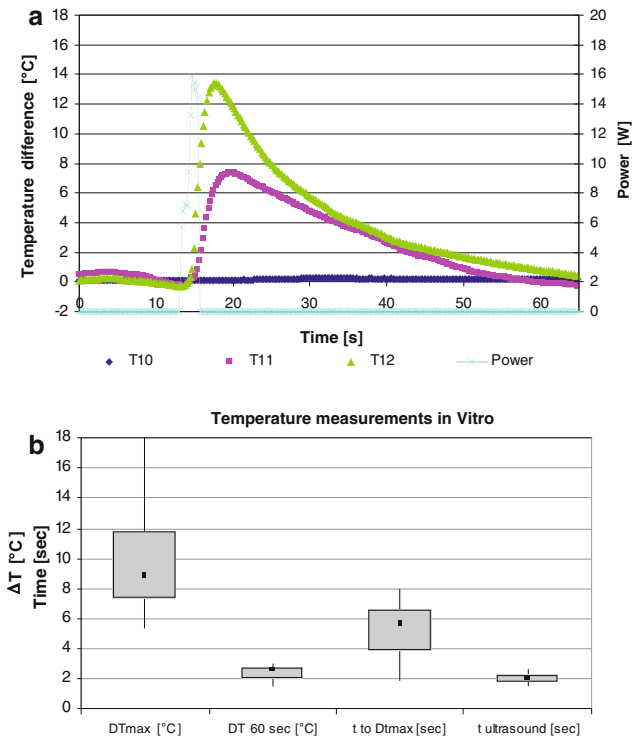

Fig. 9 Results of the in vivo temperature measurements during insertion of **a** Ø 3.5 mm polymer pin using BoneWelding® technology. **a** A typical temperature record graph and **b** data displayed in box plot format

assume that it may be related to surgical technique, such as a too slow introduction of the pins during ultrasound application provoking an early fusion between plate and screws. Nevertheless, even if implants were not completely inserted in 5/12 pins of group A, stability of the triangular plates was still given and no signs of implant loosening were detected, neither radiologically or histologically. In fact, the BoneWelding® technology may offer an advantage compared to screws which are not completely inserted. While a partially inserted screw is expected to become loose over time, the melting of the polymer into the adjacent bone may still provide enough anchorage to secure mechanical stability [55]. In addition, fusion of the plate and pins may create a "locking" function such that overall stiffness of the implant system is increased similar to the locking screw system as nowadays commonly used in metal implants (LC-plate system, Synthes Inc. Paoli, USA) [56–58].

Histology confirmed earlier studies with BoneWelding® technology, where high biocompatibility of the implants and tolerance to the insertion technology was demonstrated in the proximal tibia [3], pelvis [1] and the jaw [9] of sheep, or in clinical cases in human maxillofacial surgery [2, 23]. Differences to controls were minimal, where the same material was used but conventional insertion of screws was applied. In both instances newly formed and mineralized bone was found lining the implants independent of implant or insertion type. Furthermore, the width of bone remodeling was very similar between test groups and controls and did not even differ significantly in the central areas between implants compared to the more peripheral areas. Especially in the larger bulk implants (group A and B) new bone formation was also found between the triangular plates and bone surface, as well as in the adjacent bone cavities, more so in the opened cavities adjacent to screws. These phenomena can easily be explained by the absence of melted polymer in those cavities as compared to the pins that were inserted with ultrasound. The melted polymer intruded into those cavities providing immediate stability, however, also inhibiting new bone formation until degradation of implants occurred. However, the intrusion of polymer into the nearby opened cavities is not expected to delay bone healing in case of vertebral fractures, since it would be only in the immediate environment of the pins. Cellular reaction to all types of implants and also insertion technology was minimal and consisted of cell types that are not only expected with physiological healing of bone lesions alone [59–62], but also in conjunction with degradable biomaterials [63–65]. Macrophages and giant foreign body cells are the cells that are responsible for material degradation. As long as they are not accompanied by excessive fibrous capsule formation, clusters of lymphocytes and plasma cells leading to granuloma formation, their presence does not jeopardize overall biocompatibility [65, 66]. In the current study, no capsule formation and only very low scores of inflammatory cells including macrophages and giant foreign body cells were found, again independent of implant or insertion type. This was even true, when implants were inserted parallel and close to each other (group A), or almost touching at the tips (group B). A slight increase of eosinophils was detected in suture anchors (group C), which most likely was due to the suture material rather than the polymer pins or screws, especially when their small bulk size is considered. Last but not least, pins or screws intruding into the vertebral foramen did not cause significant damage to the included structures, such as the nerve, veins or arteries.

Temperature measurements during insertion confirmed earlier studies in cadaver bones [3, 46], where no significant increase was observed. Even though maximal temperature increase was 11.3°C, it was only for a very short duration (<1 s) and is not expected to significantly damage the adjacent bone. Also it may be assumed that the most superficial layer of cells was already damaged through preparing the hole despite flushing and cooling with saline during drilling [58, 67–69]. Bone has a rather low heat conductivity. Therefore, only a very small seam of bone cells may be subjected to this low melting heat. Compared

to the polymerization temperature found in methylmetacrylate bone cements [70–74], this temperature increase can be completely neglected as confirmed by histological findings.

In conclusion, the BoneWelding® technology offers an attractive alternative for spine surgery to more conventional methods of fixing implants to the vertebral bodies using polymer screws. The concepts of fixing triangular polymer plates with polymer pins, using single or converging pins for fracture fixation or suture anchors to attach soft tissue using ultrasound to solubilize the surface at the implant-bone surface proved valid, easy to apply, safe for the vertebral structures and biocompatible for the adjacent bone, at least at a 2-month follow-up as in the current study. Long-term application with the same material was already performed in an earlier study of our group, such that no further complications regarding biocompatibility can be expected also in longer follow-ups [3]. Future clinical or experimental studies will have to show its successful application for either fracture fixation, fusion of vertebral bodies or as suture anchor device in open laminectomy procedures.

Acknowledgments The authors are very thankful for the excellent histology sections prepared by Sabina Wunderlin, and also acknowledge SpineWelding AG for funding the study, the technical support and providing the implants and special instruments.

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